EXHIBIT 15

Amendment Under 37 C.F.R. § 1.116
Expedited Procedure – Art Unit 1651

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Confirmation No.: 4326
HO *et al.*	Art Unit: 1651
Appl. No.: 09/960,244	Examiner: Leon B. Lankford, Jr.
Filed: September 21, 2001	Atty. Docket: 2560.0020000/JAG/D-S
For: **Cell Populations Which Co-Express CD49c and CD90**	

Amendments Under 37 C.F.R. § 1.116

Mail Stop AF

Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

In reply to the Office Action dated March 27, 2009 (PTO Prosecution File Wrapper Paper No. 20080318), Applicants submit the following Amendments and Remarks.

Amendments to the Specification begin on page 2 of this paper.

Amendments to the Claims begin on page 5 of this paper.

Remarks and Arguments begin on page 7 of this paper.

It is not believed that extensions of time or fees for net addition of claims are required beyond those that may otherwise be provided for in documents accompanying this paper. However, if additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

Amendments to the Specification

Please amend the paragraph in Example 1, beginning on line 18 of page 26 and bridging to page 27, line 8 of the specification as follows:

Resuspended cells (approximately 10^6) were aliquoted into12x75 mm Flow Cytometry tubes and repelleted at 500 x g for 5 minutes. The HBSS was removed and 25 mL of the following antibodies (all obtained from Becton Dickenson), alone or in combination, were placed into each tube: mouse IgG1k FITC or -PE (clone MOPC 21) CD49c-PE (cl. C3II.1), CD90-FITC (cl. 5E10), CD45-FITC or -PE (cl. HI30). Tubes were gently vortexed and incubated for 30 minutes at 4°C. Cells were then washed in HBSS/1% bovine serum albumin, centrifuged (30 min, 4°C) and the resulting cellular pellet fixed by the addition of 250 microliters of 2% paraformaldhyde/HBSS. Flow cytometric analysis was performed employing a Becton Dickenson FACSVantage SE cytometer and analyzed using CELLQUEST® software. Figure 1 depicts results representing data collected from 2,500-10,000 events per panel. After compensation for non specific antibody staining using mouse IgG1 isotype controls, cellular expression of CD45, CD49c and CD90 in the cultured bone marrow cells was assessed. The adherent population derived from mononuclear cells initially purified using ammonium chloride lysis contained approximately 70% CD49c positive cells at a similar stage of culture (Figure 1A). The majority of cells that did not express CD49c were positive for expression of hematopoetic/myeloid lineage marker CD45 (Figure 1A, LR quadrant), demonstrating that the CD49c positive cell population derived from human bone marrow isolated was not directly related to known hematopoietic precursors. More than 94% of the adherent population was CD90 and CD49c positive (Figure 1B).

Please amend the paragraph in Example 2, beginning on line 27 of page 27 and bridging to line 6 of page 28 of the specification as follows:

Cytometry analysis of the CFU generated showed that approximately 50% of the adherent population expressed the marker CD49c at 7 days in vitro (Figure 2A, sum of UL and UR quadrants). The majority of cells that did not express CD49c were positive for expression of hematopoetic/myeloid lineage marker CD45 (Figure 2A, LR quadrant), demonstrating that the CD49c positive cell population derived from human bone marrow isolated by this procedure was not directly related to known hematopoietic precursors. More than 91% of the adherent population was CD90 and CD49c positive (Figure 2B).

Please amend the paragraph in Example 3, beginning on line 22 of page 28 of the specification as follows:

The purity of the cells (percentage of cells which co-express CD49c/CD90) in the Master Cell Bank was determined by flow cytometry ***using the same method as above.*** ~~More than 94% of the adherent population was CD90 and CD49c positive (Figure 1B).~~ The vast majority (>98%) of the resulting population expressed CD49c (Figure 1C) and virtually lacked any expression of the myeloid related marker CD45 (Figure 1C, LR quadrant). Thus, the expansion procedure as described herein produces a substantially homogenous population of adherent cells which co-express CD49c and CD90 and lack significant expression of the marker CD45.

Please amend the paragraph in Example 3, beginning on line 1 of page 29 of the specification as follows:

Similarly, the master cell bank generated from the CFU derived using the method of Example 2 showed that ~~more than 91% of the adherent population was CD90 and CD49c positive (Figure 2B) and~~ the majority of cells (>98.8%) of the resulting cell population expressed CD49c (Figure 2C) and virtually lacked any expression of the myeloid-related

marker CD45 (Figure 2C, LR quadrant). Thus, the expansion procedure as described herein generates a substantially homogenous population of adherent cells which co-express CD49c and CD90 and lack significant expression of the marker CD45.

Amendments to the Claims

The listing of claims will replace all prior versions, and listings of claims in the application.

1-13. (Cancelled).

14. (Previously Amended) An isolated cell population derived from human bone marrow, wherein greater than about 91% of the cells of the cell population co-express CD49c and CD90, and wherein the cell population maintains a doubling rate of less than about 30 hours after 30 cell doublings.

15-20. (Cancelled).

21. (Previously Amended) The isolated cell population of Claim 14, further including expression of p21 or p53 after between about 20 to about 50 population doublings of the cells, wherein expression of p53 is a relative expression of up to about 3000 transcripts of p53 per 10^6 transcripts of an 18s rRNA and expression of p21 is a relative expression of up to about 20,000 transcripts of p21 per 10^6 transcripts of an 18s rRNA.

22-24. (Cancelled).

25. (Previously Amended) The isolated cell population of Claim 14, wherein the cell population does not express CD34 and/or CD45.

26. (Previously Amended) The isolated cell population of Claim 14, wherein the cell population further expresses at least one trophic factor selected from the group consisting of BDNF, IL-6, NGF and MCP-1.

27-96. (Cancelled).

97. (Currently Amended) An isolated cell population obtainable from human bone marrow by steps that comprise:

a) incubating human bone marrow cells under a low oxygen condition of about 5% oxygen such that said cells when allowed to adhere to a tissue culture-treated surface will produce adherent colony forming units (CFU); and,

b) passaging cells in said adherent CFU at a seeding density of ~~less than about 2500~~ about 30 cells/cm^2,

wherein greater than about 91% of said passaged cells co-express CD49c and CD90, and wherein said passaged cells maintain a population doubling rate of less than about 30 hours after 30 cell doublings.

Remarks

Entry of the foregoing amendments in the specification and claims is requested pursuant to 37 C.F.R. § 1.116(b)(2) & (b)(3).

The specification is amended herein pursuant to 37 C.F.R. § 1.116 (b)(3). In particular, the specification has been amended to cancel a previous amendment wherein a sentence reading "More than 94% of the adherent population was CD90 and CD49c positive (Figure 1B)" from Example 1" was moved from the paragraph beginning on line 18 of page 26 and bridging to page 27, line 8 to Example 3, in the paragraph beginning on line 22 of page 28. The previous amendment was objected to by the Examiner as allegedly introducing new matter. On June 16, 2009, Applicants filed a Petition Under 37 C.F.R. § 1.181 requesting reconsideration of the Examiner's objection. Applicants' petition was denied pursuant to a decision mailed July 14, 2009. Therefore, Applicants submit the present amendment to cancel the alleged new matter by deleting the sentence from the location where it was placed via the previous amendment and inserting this sentence in the same location in the specification as originally filed.

Likewise, the specification is amended herein to cancel the previous parallel amendment of Example 3 by deleting the phrase "more than 91% of the adherent population was CD90 and CD49c positive (Figure 2B) and" from the paragraph beginning on line 22 of page 28 and inserting this phrase in original sentence form ("More than 91% of the adherent population was CD90 and CD49c positive (Figure 2B)") in the same location in the specification as originally filed (*i.e.*, in Example 2, beginning on line 27 of page 27 and bridging to line 6 of page 28).

No new matter has been added.

Applicants note that these amendments could not have been introduced earlier because the first objection to the alleged new matter was not asserted by the Examiner until mailing of the currently pending final office action and Applicants only thereafter were able to obtain a subsequent disposition from the U.S.P.T.O. based on Applicants' Petition under 37 C.F.R. § 1.181.

Claim 97 is amended herein pursuant to 37 C.F.R. § 1.116(b)(2). In particular, the Examiner has rejected claim 97 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. In particular, the Examiner has rejected claim 97 based on recitation of "low oxygen" allegedly because "it is unclear what the intended metes and bounds of a 'low oxygen' condition are." *See*, Final Office Action, page 5, last two paragraphs.

Pursuant to 37 C.F.R. § 1.116(b)(2), in the interest of presenting rejected claim 97 in better form for consideration on appeal (but without acquiesence or disclaimer of claims encompassing a low oxygen condition which is less than atmospheric oxygen), Applicants have herein amended claim 97 to be drawn to an isolated cell population obtainable by a process comprising incubating human bone marrow cells under a low oxygen condition *of about 5% oxygen*. Support for this amendment can be found in the specification as originally filed, for example, at: page 8, lines 11-12; page 12, line 1; page 15, line 8; and, Example 3, page 28, lines 18-19.

The Examiner has also rejected claim 97 under 35 U.S.C. § 112, first paragraph, as allegedly "failing to comply with the written description requirement." The Examiner states that "New claim 97 is rejected for containing new matter" because "[t]he examples cited for support do not contain the limitation of a seeding density of 'less than about 2500 cells/cm^2..." *See*, Final Office Action, page 5, first and second paragraphs.

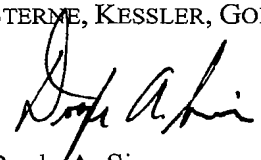
Pursuant to 37 C.F.R. § 1.116(b)(2), in the interest of presenting rejected claim 97 in better form for consideration on appeal (but without acquiesence or disclaimer of claims encompassing seeding densities of less than about 2500 cells/cm^2), Applicants have herein amended claim 97 to be drawn to an isolated cell population obtainable by a process comprising passaging cells at a seeding density of about 30 cells/cm^2. Support for this amendment can be found in the specification as originally filed, for example, at page 3, lines 13-17; page 12, lines 4-7; Example 3, page 28, lines 16-17; and, Example 4, page 29, lines 12-13.

Conclusion

Applicants respectfully request entry of the amendments in the specification and claims presented herein to simplify the issues necessary for consideration upon appeal.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



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